heterocyclyl, alkoxyalkyl, aryloxyalkyl, alkoxycarbonyl, aryloxycarbonyl, cycloalkyloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl groups; Y represents O or S; Z represents oxygen, sulfur or $NR^{10}$, where $R^{10}$ represents hydrogen or substituted or unsubstituted groups selected from $(C_1\text{-}C_{12})$alkyl, aryl, ar$(C_1\text{-}C_{12})$alkyl, hydroxy$(C_1\text{-}C_{12})$alkyl, amino$(C_1\text{-}C_{12})$alkyl, heteroaryl, heteroar$(C_1\text{-}C_{12})$alkyl groups; $R^8$ represents hydrogen, substituted or unsubstituted groups selected from $(C_1\text{-}C_{12})$alkyl, aryl, ar$(C_1\text{-}C_{12})$alkyl, heteroaryl, heteroar$(C_1\text{-}C_{12})$alkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, alkoxyalkyl, alkylaminoalkyl groups when Z represents sulfur or $NR^{10}$; while $R^8$ represents substituted or unsubstituted groups selected from $(C_1\text{-}C_{12})$alkyl, aryl, ar$(C_1\text{-}C_{12})$alkyl, heteroaryl, heteroar$(C_1\text{-}C_{12})$alkyl, heterocyclyl, heterocyclylalkyl, hydroxyalkyl, alkoxyalkyl, alkylaminoalkyl groups, *when Z represents O*; $R^{10}$ and $R^8$ together may form a 5 or 6 membered substituted or unsubstituted cyclic ring structure containing carbon atoms or containing one or more heteroatoms selected from O, N and S, to a further compound of formula (I), where all symbols are as defined earlier and Y & Z represents oxygen and $R^8$ represents hydrogen.

B4 con.

~~ii. Removing any protecting group;~~

iii. Resolving the racemic mixture into pure enantiomers by the known methods and

iv. Preparing a pharmaceutically acceptable salt of a compound of formula (1) and/or a pharmaceutically acceptable solvate thereof.

---

## REMARKS

- **Present Application**

Claims 1 – 9, 13, 14, 18, 19, 21 – 27[2], 36, and 37 are now pending in this application. Applicant respectfully asserts that all of these claims are patentable. Accordingly it is respectfully urged that allowance of this application is in order. Early notification of the allowability of the claims is courteously solicited.

- **Final Election/Restriction Requirement**

  - **The Examiner's Position**

The Examiner argues the inventions in Groups I, IV and VII are related as mutually exclusive species in an intermediate-final product relationship (page 2 of the Office action), that

---

[2] Listed erroneously as 11 – 17 under the header "Detailed Action" at page 2 of the Office Action.

Groups I, V and VI are related as a process of making and product made (page 2 of the Office Action), and that Groups I and II are related as product and process of use (page 3 of the Office Action). The Examiner further asserts that "the merit of patentability" of Group IX "is on the dosage and kind of specific ingredients and their activity functioning together" (page 3 of the Office Action).

- **The Applicants' Response**

Applicants acknowledge the Examiner's rejection of their traverse of the Examiner's restriction requirement set forth in Paper No. 5, and the requirement being made FINAL. Applicants respectfully reserve any right to contest such FINAL requirement by petition under 37 C.F.R. 1.144.

- **Response to Objections**

  - **The Examiner's Position**

The Examiner has issued several objections. Claim 36 is objected to because it depends from canceled claims in steps b, c, d, e and f.. Claims 2 – 9 , 12, 14, 22, 24 – 27 are objected to for being dependant on a rejected claim. Appropriate correction is required.

  - **The Applicants' Response**

Claim 36 has been amended to delete the now inappropriate dependency (the dependency on claims withdrawn in response to the restriction requirement). As the independent claims from which dependent claims 2 – 9, 12, 14 22 and 24 – 27 depend have each been amended to overcome the Examiner's rejections, it is asserted that the objection to such claims are also overcome.

- **Response to Rejections**

  - **35 U.S.C. §112, First Paragraph**

    - **The Examiner's Position**

The Examiner has rejected claims 1, 18, 36 and 37 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification "in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention" (page 4, paragraph 1, of the Office Action). Applying the factors set forth in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988), the Examiner asserts that that specification in particular fails to enable the skilled artisan to practice the invention without undue experimentation. The Examiner argues that "[t]here is little predictability in the art of which modifications may be made to the claimed compound which would retain its ability to be useful in treating obesity, hyperlipidemia, and atherosclerosis" (page 5, paragraph 1, of the Office Action).

In regard to claim 18 the Examiner asserts that the specification does not enable a person skilled in the art based on the testing protocol disclosed to use the invention to identify compounds useful in the treatment of the "vast number of diseases caused by hyperlipidemia, hyperchloesteremia, hyperglycemia, obesity, impaired glucose intolerance, leptin resistance, insulin resistance, (and) diabetic complications" given the unpredictability of the art, and the many causative agents of such conditions. In short, the Examiner asserts that the claimed invention would require undue experimentation.

Similarly with respect to claim 37, the Examiner asserts that the specification lack positive steps which teach how to "convert a compound of formula (1) into a further compound of formula (1)," "resolving the racemic mixture into pure enantiomers by the known methods," and "preparing a pharmaceutically acceptable salt of a compound of formula (1) and/or a pharmaceutically acceptable solvate thereof" are preformed. Asserting little predictability in the art, the Examiner asserts that numerous amount of modifications would need to be performed in the processes to obtain the claimed compound. The Examiner iterates, however, that such rejections "can be overcome by Applicant deleting the terms derivatives, analogs, and

ploymorphs in claim 1, deleting the term "preventing" in claim 18, and listing positive process steps in claim 37" (page 7, paragraph 1, of the Office Action).

- **The Applicants' Response**

Applicants respectfully traverse the Examiner's 35 U.S.C. §112, first paragraph, rejections based in part upon its assertion that the specification contains a written description of the manner and process of making and using the embodiments of the invention asserted in the claims, in such full clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. It is asserted that the specification teaches those in the art enough that they can make and use the invention without 'undue experimentation.'" *Amgen v. Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc.*, Slip Opinion (Fed. Cir. January 6, 2003). Applicants note that a patent need not disclose that which is already known in the art in order to be enabling *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Even when "considerable amount of experimentation" is necessary to eventuate in the invention such is permissible when the experimentation was "merely routine, or if the specification in question provide[d] a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996)

However, in order to expedite prosecution in this case to gain the earliest allowance to claims of present commercial interest, Applicant has deleted the terms derivatives, analogs and polymorphs in claim 1, deleted the term "preventing" in claim 18 and listed positive process steps in claim 37, in accord with the Examiner's suggestion set forth at page 7 of the Office Action. Given these changes, and the Examiner's acknowledgement that such changes would overcome these 35 U.S.C. §112, paragraph 1, rejections, Applicants assert that the claims are now in condition for allowance. In making such amendments, Applicants expressly reserve the right to prosecute the unamended claims in a future continuation, continuation-in-part, divisional, etc. application.

**35 U.S.C. §112, Second Paragraph**

- **The Examiner's Position**

The Examiner has rejected claims 19, 23, 36 and 37 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. The Examiner asserts confusion with respect to: (1) claim 19, line 7: the use of the redundant abbreviation PCOS; (2) claim 23: the species listing in particular in regard to what "and its Li, Na, K, Ca, Mg, lysine, arginine guanidine and its derivatives" modifies; (3) claim 36: the preamble fails to clarify that the steps of the claim related to different processes for preparing a compound of formula (I); (4) claim 37: in failing to define what a "further compound of formula (I)" relates to and in the use of and/or making it unclear whether or not a pharmaceutically acceptable solvate is prepared with a pharmaceutically acceptable salt. The Examiner suggest the deletion of "and/or" and insertion in its stead of "and optionally" (pages 8 – 9, of the Office Action).

- **The Applicants' Response**

Applicants respectfully traverse such rejections based in part upon the assertion that one of ordinary skill in the art would read the claims as particularly pointing out and distinctly asserting the subject matter of the embodiment claimed.

However, the Applicants have amended the claims in a manner which they believe overcome each of the Examiner's 35 U.S.C. §112, paragraph 2, rejections. With respect to claim 19, the abbreviation (PCOS) has been removed. With respect to claim 23 the term "and its derivatives" has been removed from the claim and the wording has been clarified following each species to clarify that the recitation "and its Li, Na, K, Ca, Mg, lysine, arginine, guanidine" references the species preceding it. The preamble to claim 36 has been clarified to indicate that each step recited thereafter is a different processes that may be used in the preparation of a compound of formula (I), claim 37 has been amended to indicate that it asserts the process according to the claim 36, comprising the carrying out one or more of delineated optional steps. The phrase "a further compound of formula (1)" has been removed. Lastly in regard to claim 37 the term "and/or" in step iv has been replaced by the phrase "and optionally" as suggested by the Examiner.

## CONCLUDING REMARKS, REQUESTS AND FEE PAYMENTS

For all of the reasons set forth above, it is firmly believed that pending claims 1 – 9, 13, 14, 18, 19, 21 – 27, 36 and 37 are allowable. Early notification of allowance is courteously solicited.

### Fees

Applicant petitions for a two-month extension of time in which to reply to the outstanding office action. Applicant has enclosed a check in the sum in accord with 37 C.F.R. 1.17(a)(2) for a large entity. While it is believed that such check covers all sums due, the Assistant Commissioner is authorized to charge payment of any fees that may be required under 37 C.F.R. §1.16 in connection with the paper(s) transmitted herewith, or credit any overpayment of the same, to Deposit Account No. 033-975.

Respectfully submitted,

Date: April 28, 2003

Steven J. Moore, Reg. No. 35,959
Attorneys for Applicants
Pillsbury Winthrop LLP
1600 Tysons Boulevard
McLean, VA 22102
(203) 965-8254